REMARKS

Claims 1-3, 7-17, 25-42 and 44 were pending. Applicants have added new claim 45. Support for this amendment can be found throughout the specification as filed, for example, at Example 17, and thus no new matter is added. Claims 1-3, 7-17, 25-42 and 44-45 are pending and under consideration.

35 U.S.C. § 103(a) – Obviousness

Claims 1-3, 7-17, 25-42 and 44 remain rejected under 35 U.S.C. § 103(a) as obvious over Gewirtz et al., in view of Patel et al., Sachetto et al., Yacyshyn et al. and Bennett et al. (US 6,096,722) for the reasons of record. Applicants respectfully traverse.

Lack of a prima facie *case of obviousness*

The pending claims are directed to a method of treating pouchitis in a human by rectally administering a pharmaceutical composition comprising an antisense oligonucleotide having the nucleobase sequence recited in SEQ ID NO: 1. To establish that this method is *prima faice* obvious, it is the Office's burden to demonstrate that the cited references provide a reasonable expectation of success, or a that the results are predictable – Applicants do not have to establish a lack of an expectation of success or unpredictability. *See M.P.E.P. §2143.* Applicants submit that the Office has failed to establish a *prima facie* case of obviousness for at least the reason that it has failed to meet its burden of establishing that there is a likelihood of success or predictable results.

Gewirtz, the primary reference relied on by the Office, indicates that the therapeutic value of alicaforsen is unproven and unknown, and that additional clinical trials were necessary "before any reasonable assessment of its value" for treating Crohn's Disease could be made – it provides no evidence that alicaforsen can treat pouchitis. Thus, Gewirtz does not provide a basis for a reasonable expectation of treating pouchitis using an enema formulation of alicaforsen.

While Patel discloses that plasma soluble ICAM-1 levels are elevated in active pouchitis, the authors conclude that "inhibition of these leucocyte-endothelial cell interactions might cause decreased leucocyte transmigration to the site of inflammation and could, hypothetically, provide a new target for the control of inflammatory bowel disease." *Patel* at page 1040, final sentence

(emphasis added). The authors provide a suggestion for further investigation, but a "hypothetical" new target for treatment is not a basis for a reasonable expectation of success.

Sachetto discloses a modest effect of a xantham gum enema on pouchitis scores, but the authors' assertion that the disclosed treatment for pouchitis is effective for UC or CD is not supported by any evidence. In addition, given the differences in standard treatments for UC or CD and pouchitis (see previous responses and exhibits), one of skill in the art would not conclude that UC or CD anti-inflammatory treatments are generally interchangeable with those of pouchitis, even if one accepted the unsupported assertions of Sachetto regarding xantham gum and HPMC enemas' effectiveness for UC and CD.

Yacyshyn discloses modest effects of i.v. infusion of alicaforsen in patients with CD. However, the reference does not provide any guidance or data regarding administration of alicaforsen as an enema for treating pouchitis.

Bennett discloses data similar to Yacyshyn – i.v. infusion of ISIS 2302 results in modest improvement for patients with CD. Bennett also discloses examples of enema formulations of ISIS 2302, and states that enema administration "is being pursued in patients with disease of the left colon [ulcerative colitis], which is accessible by enema." *Bennett* at col. 71, lines 35-34. However, Bennett does not disclose any data showing that enema administration of ISIS 2302 is effective for treating any disease, including UC, CD or pouchitis.

These references, alone or in combination, do not provide a factual basis to conclude that there is a reasonable expectation of success. While there is mixed evidence that i.v. infusion of ISIS 2302 (alicaforsen) can provide some relief to patients with CD, none of the references provide any evidence that enema administration of ISIS 2302 could successfully treat any disease – CD, UC or pouchitis. The Office has not established that changing the route of delivery from i.v. infusion to enema is a simple substitution which yields predictable results. Thus, it is not established that an enema formulation of ISIS 2302 would work for CD, let alone pouchitis.

The fact that plasma levels of soluble ICAM-1 are elevated in active pouchitis provides a "hypothetical" reason that targeting ICAM-1 could be a new therapy according to Patel – but this is nothing more than an invitation to experiment. If elevated ICAM-1 levels were sufficient to make anti-inflammatory therapies for CD, UC and pouchitis interchangeable, one would expect the standard anti-inflammatory treatments for UC and CD to work on pouchitis just as well – but

they don't. This is the reason that standard anti-inflammatory treatments for UC and CD are not the recommended treatment for pouchitis (see previous responses and exhibits). Thus, the fact that these diseases share a marker of inflammation (elevated ICAM-1) isn't a sufficient basis to believe that targeting ICAM-1 using an enema would have a reasonable expectation of success in treating pouchitis.

Applicants remind the Office that in establishing a *prima facie* case of obviousness, it is the Office's burden to demonstrate that the cited references provide a reasonable expectation of success, or a that the results are predictable – Applicants do not have any burden to establish a lack of an expectation of success. *See M.P.E.P. §2143.* As the results of i.v. infusion of ISIS 2302 for CD are mixed, as no reference discloses the successful use of an ISIS 2302 enema for treating any disease, and, as the standard anti-inflammatory treatments for CD and UC are not the recommended treatment for pouchitis, the mere fact that ICAM-1 is elevated in CD, UC and pouchitis is not sufficient to meet the Office's burden of demonstrating a reasonable expectation of success. Thus, even if *arguendo* it may have been reasonable or obvious to try treating pouchitis with an enema formulation of ISIS 2302, this is not sufficient to establish a *prima facie* case of obviousness – the Office has failed to articulate "a finding that one of ordinary skill in the art could have pursued the known potential solution with a reasonable expectation of success." *M.P.E.P. §2143 E.*

Unexpected Results

Even if the Office has established a *prima facie* case of obviousness, a point Applicants do not concede, Applicants submit that the claimed methods have unexpected results that are sufficient to demonstrate nonobviousness.

The results reported in Example 17 of the instant specification demonstrate that treatment with an enema formulation of antisense targeting ICAM-1 resulted in remission of 58% of patients. A month after treatment ended, 50% of the patients were still in remission. This is particularly surprising because the patients being treated were suffering from chronic, unremitting pouchitis that was unresponsive to conventional therapies. *See Specification* at ¶ [0320]. Thus, Applicants have provided a successful treatment for a chronic disease that currently has no conventional therapy available – a treatment which is successful in nearly two-

thirds of the patients tested, and which maintains remission for at least a month after treatment ceases. None of the cited references provide a basis for expecting such a successful outcome using an enema formulation of an antisense oligonucleotide to treat chronic, unremitting pouchitis.

The Office responds by arguing that: 1.) the inventors are not the first to recognize the need for a treatment; 2.) Sachetto provides an additional therapy option; 3.) reducing PDAI scores in patients unresponsive to conventional therapy is not "particularly suprising" because there is "at least one other pouchitis treatment method in the art," presumably Sachetto; 4.) the results are expected because ISIS 2302 "was reasonably expected to have some therapeutic effects" given ICAM-1 levels are elevated in active pouchitis, and because ISIS 2302 reduced inflammation in CD and UC patients; 5.) the results of 50-58% remission "are not commensurate in scope with the claims" because the claims do not recite increasing remission rates; 6.) the results are not surprising because "it was known that ISIS 2302 was capable of increasing remission rates" in IBD such as CD, citing Bennett and Yacyshyn; and, 7.) nothing in the cited references suggests "that the failure of ISIS 2302 in pouchitis treatment is highly likely or is reasonably expected," rather, the references provide a "reasonable expectation of success..." *Office Action* at 17-19.

Regarding point 1.), it is not relevant to Applicants' assertion of unexpected results. Applicants need not be the first to recognize the need for a pouchitis treatment for their solution to have surprising results. The results need only be unexpected in view of the closest cited art. The Office's assertion of a long-felt need, is however, further evidence of non-obviousness. *See M.P.E.P. § 716.04.* Thus, rather than supporting the Office's claim of obviousness, the Office's assertion that "the non-responsive, unsatisfactory, conventional therapeutic strategy for treating pouchitis ... has long been recognized in the art..." is further evidence of non-obviousness. *Office Action* at 17 (emphasis added).

Regarding points 2.) and 3.), Applicants submit that no other conventional, approved or art recognized solution was available. In addition, the results obtained using the claimed method are unexpected and superior to those of Sachetto. Sachetto does not provide any basis to expect that antisense oligonucleotides, or ICAM antisense in particular, would be able to treat pouchitis because it does not disclose the use of antisense to treat any disease, or the administration of

antisense by enema. In addition, Sachetto reports that only 9 of 20 patients (45%) showed a reduction in PDAI of 3 points or more. The median PDAI score of those who completed treatment was 9. This means that more than half the patients that completed treatment were not in remission, which is defined as having a PDAI score of less than 7. Clearly, Applicants result of a remission rate of 58% is superior and unexpected in view of Sachetto.

Regarding point 4.), even if *arguendo* "some therapeutic effects" of ISIS 2302 were expected as the Office asserts, this does not rebut Applicants' claim that a 58% remission rate is unexpected in view of the closest cited reference. The unexpected results do not have to be "contrary or conflicting with the teachings of the prior art" as alleged by the Office. *Office Action* at page 18. The Office's assertion that "some therapeutic effect" was expected is not a sufficient response to Applicants' evidence. The Office must demonstrate that one of skill in the art expected that the claimed method would result in a 58% remission rate in patients with chronic, unremitting pouchitis that was not responsive to conventional therapy.

Regarding point 5.), Applicants remind the Office that unexpected results do not need to be recited in the claims. If the unexpected properties of a compound or method must always be recited in a claim, they would not be "secondary considerations" which can overcome a *prima facie* case of obviousness, but rather would always be limitations which are considered as part of the *prima facie* case. *See, e.g. M.P.E.P. §2145.* Rather, the unexpected results that flow from the claimed composition or method need only be unexpected in view of the closest cited reference. *See M.P.E.P. §716.02.*

Regarding point 6.), Applicants are unsure which reference, Bennett or Yacyshyn, the Office views as the closest cited reference. However, regardless of which reference Applicants' results are compared to, a 58% remission rate is unexpected and surprising. As noted previously, both Bennett and Yacyshyn are treating CD, not pouchitis. As the Office has acknowledged, pouchitis is a distinct disease from CD, even *if* both are IBDs. The fact that a treatment for CD cannot be assumed to work as well in pouchitis is evident from the fact that standard anti-inflammatory treatments for CD are not recommended for pouchitis – in spite of the fact that they share elevated levels of ICAM-1. In addition, both references administered the alicaforsen by i.v. infusion, not rectally. One of skill in the art will recognize that there are significant differences between systemic delivery by i.v. infusion, and local topical administration via the rectum, and

that success in one route of administration does not mean success in the other. Otherwise, Bennett and Yacyshyn would have started with an enema formulation for CD, since Gewirtz teaches that it is "more desirable." In sum, neither Bennett nor Yacyshyn, regardless of which reference the Office chooses as the closest cited reference, provides an expectation of a 58% remission rate for the claimed method.

Nor are the results of Bennett or Yacyshyn sufficient to counter Applicants' assertion of unexpected results. While the results of Example 17 are not directly comparable to those of Bennett and Yacyshyn, Bennett reports that 47% CD patients were in remission following treatment, and Yacyshyn discloses that only 41% of CD patients administered alicaforsen by i.v. infusion experienced remission at the end of treatment. Combined, this is a remission rate of only 44%. In contrast, Ex. 17 discloses that 58% pouchitis patients were in remission following treatment. Applicants reiterate that these results are not directly comparable, given the differences in the kind of disease, the intensity of the disease, drug co-therapy, the amount and route of antisense administration, and length of treatment. Never the less, a 58% remission rate for Ex. 17 is better than the 47% or 41% remission rates reported in Bennett and Yacyshyn. This is unexpected, since nothing in Bennett, Yacyshyn, or the other references suggests that ISIS 2302 as an enema would perform better in treating pouchitis than it did in treating CD when administered by i.v. infusion.

Finally, Applicants address point 7.), that nothing in the cited references suggests "that the failure of ISIS 2302 in pouchitis treatment is highly likely or is reasonably expected," rather, the references provide a "reasonable expectation of success..." *Office Action* at page 19. Again, the Office's asserted standard is not the proper one. Applicants do not need to demonstrate that the failure of ISIS 2302 as an enema was "highly likely or is reasonably expected" for Applicants' results to be unexpected. Even if, *arguendo*, there was an expectation of "some therapeutic effects" as asserted by the Office, the results are unexpected. A result where nearly 2 out of 3 patients that were unresponsive to conventional therapy went into remission – not merely improved, but remission – is unexpected. These results constitute more than merely "some therapeutic effect." Such an outstanding result is a solution to what the Office has acknowledged was a long-felt need, and represents a significant improvement for patients suffering from this serious disease.

Response to Office's Arguments

Applicants clarify their previous responses, and to respond to the Office's remarks in the pending Office Action.

The Office states that "there is nothing [in Gewirtz] whatsoever that indicates that there would have been no reasonable expectation such that one would not have expected any therapeutic effect of alicaforsen in an enema formulation." *Office Action* at page 3. Similarly, the Office states that "[t]here is nothing that suggests from the 'considerably effective' study that alicaforsen in an enema formulation would not have been effective in treating CD." *Id.* at page 4.

Applicants respectfully submit that this is not the proper standard. It is the Office's burden to demonstrate that there is a basis for one to reasonably expect success. The absence of any reason to expect failure, even if it were true, does not satisfy the Office's burden. The Office must articulate a reason one of skill in the art would believe that there is a reasonable expectation of success at treating pouchitis using an enema formulation of ISIS 2302. It is not Applicants' burden to show evidence of an expectation of failure.

The Office attempts to argue that there is a reasonable expectation of success for enema formulations, arguing that:

> [T]he fact that Gewirtz et al. did explicitly suggest that establishing effective enema dosing "would be considerably more desirable" and that alicaforsen remains to be "promising" [*sic*] for treating inflammatory bowel diseases although enema-based alicaforsen was "unproven" does indicate a "reasonable", if not absolute, expectation of success…[of] some therapeutic effects of alicaforsen in an enema formulation for treating inflammatory bowel disease. *Office Action* at 4.

Applicants fail to see how a suggestion that an enema formulation is "desirable" but "unproven" could possibly provide a reasonable expectation of success. This is nothing more than an invitation to those of skill in the art to pursue an enema formulation because it is "more desirable." The Office has not pointed to any portion of the reference to support a reasonable conclusion that such an endeavor would be successful for treating CD, yet alone pouchitis.

The Office concludes its comments regarding Gewirtz by stating that the portions of Gewirtz cited by Applicants "would not have taught away or discouraged a person of ordinary skill in the art from making and using the enema formulation of alicaforsen" for treating IBD, including UC, CD, and pouchitis. *Id.* at page 5 (emphasis added).

Again, a teaching away or discouragement is not the standard. The Office must show that even if *arguendo* one of skill in the art were motivated to treat pouchitis with an enema formulation of alicaforsen, they could do so with a reasonable expectation of success.

Regarding Sachetto, the Office objects to Applicants' characterization of the Office as "mischaracterizing" or "misstating" what Sachetto teaches. *See Office Action* at page 7. Applicants apologize for any misunderstanding. Applicants were merely noting that while Sachetto states that the described enemas can treat UC and CD, there is no evidence in Sachetto to support that assertion, as the only working example treats pouchitis, not UC or CD. Applicants also note that while the subject of Example 4 of Sachetto previously suffered from UC, they had undergone "total colectonmy with mucosal protectomy" and thus were no longer suffering from ulcerative colitis. They were in fact now suffering from pouchitis, which the Office has admitted is a distinct disease. *Sachetto* at col. 8, lines 64-67.

Regarding Yacyshyn, the Office objects to Applicants' statement that "Yacyshin [*sic*] does not support the assertion that an alicaforsen treatment for CD can lead to an alicaforsen treatment for any disease much less pouchitis," and request that Applicants support their statement with evidence. *Office Action* at page 7. Applicants were not stating that the Office has asserted that "Yacyshyn et al. suggested using alicaforsen for 'any' disease," as the Office has characterized this statement. *Office Action* at 7. Applicants apologize for any misunderstanding. Applicants point was that Yacyshyn's treatment of CD by i.v. infusion of alicaforsen does not support a conclusion that one of skill in the art can successfully treat any other disease using alicaforsen, or pouchitis in particular, because CD and pouchitis are distinct diseases with distinct therapies (see previous response and evidence).

Regarding Bennett, Applicants maintain that: 1.) the only data regarding efficacy of ISIS 2302 for treating a disease in humans is found in Example 52, where i.v. infusion of ISIS 2302 was used to treat CD; and, 2.) there is no data in Bennett regarding the efficacy of ISIS 2302 in an enema formulation for the treatment of any disease in a human. The Office apparently does not dispute this assertion.

Applicants clarify that they are not trying to "show nonobviousness by attacking references individually where the rejections are based on combinations of references." *Office Action* at page 7 and 9. Applicants are clarifying what each of the cited references teach, one

reference at a time. Applicants are free to challenge the Office's assertions regarding what each particular reference teaches or suggests to one of skill in the art, as nothing in *In re Keller* or *In re Merck & Co.* cited by the Office prohibits clarifying what a particular reference teaches. Applicants address the combination of the references in their response at pages 8-10.

At pages 12-13, the Office asserts that "the fact that reducing ICAM-1 level in a subject is a reasonably efficacious means to treat a chronic inflammatory bowel disease, combined with the fact that ISIS 2302 (an ICAM-1 inhibitor) was shown to have therapeutic values for treating CD and UC provide a reasonable 'basis' such that one can reasonably expect some treatment effects in pouchitis patients having increased ICAM-1 levels by administering a therapeutic dose of ISIS 2302." First, Applicants are not aware of any reference of record which reports that ISIS 2302 was successfully used to treat UC. Second, the results of ISIS 2302 for treating CD are mixed, and Gewirtz states that more studies are needed. Finally, if sharing elevated ICAM-1 levels were sufficient to predict success in treating a disease using an ICAM-1 inhibitor, according to the Office's logic, there is a reasonable basis that all diseases with elevated ICAM-1 levels can be treated with ISIS 2302, not just IBDs. Clearly, shared elevated ICAM-1 levels is not sufficient for treatments to be interchangeable, even between CD and pouchitis, otherwise standard anti-inflammatory treatments used in CD would work just as well in pouchitis.

Regarding the Office's discussion of Example 17 on pages 13-14 of the Office Action, Applicants cited Example 17 for support of the assertion that: "Some patients with UC or familial polyposis may undergo surgery to form an ileal pouch." Applicants submit that the Office is not permitted to use the rationale found in Applicants' specification to prove obviousness – the specification is not prior art. If the Office can use the inventors' rationale for their invention found in the specification as evidence that it was obvious, nothing in the world will be patentable, except those inventions for which the inventor had no rationale to pursue.

Applicants' arguments and exhibits regarding the conventional treatment of UC, CD and pouchitis are made to rebut the Office's assertion that because UC, CD and pouchitis are all inflammatory diseases, reducing inflammation by administering an ICAM-1 inhibitor is reasonably expected to work in all three diseases. Applicants' evidence suggests that this is not the case. If reduction of inflammation worked in pouchitis as it does in CD and UC, anti-inflammatory drugs would be the recommended treatment for pouchitis as well, but they are not.

Therefore, one of skill in the art would not assume that reducing inflammation by reducing ICAM-1 would work in pouchitis, even if it worked in CD.

Conclusion 35 U.S.C. § 103(a) rejections

None of the cited references, alone or in combination, provide a reasonable basis for one of skill in the art to expect that enema formulations comprising an antisense oligonucleotide having the nucleobase sequence recited in SEQ ID NO: 1 would successfully treat pouchitis. The Gewirtz reference states that additional data is needed before a reasonable assessment can be made of whether ISIS 2302 can successfully treat CD. Bennett does not report the successful treatment of any human disease using an enema formulation of ISIS 2302, and does not mention pouchitis. Contrary to the Office's assertions, it is clear that anti-inflammatory treatments for UC or CD are not expected to work for pouchitis, regardless of their shared symptoms and elevated levels of ICAM-1. Thus, as the results in Example 17 of the instant specification are unexpected in view of the cited references, and a *prima facie* case of obviousness was not made by the Office, the pending claims are patentable over the cited references.

Accordingly, for the reasons given above, Applicants request reconsideration of the rejection of the pending claims under 35 U.S.C. § 103(a) over the cited references.

Double Patenting

All pending claims are rejected under the doctrine of nonstatutory obviousness-type double patenting over claims 1-2 and 4-9 of copending Application No. 11/720,745. The Office asserts that although the conflicting claims are not identical, they are not patentably distinct from each other.

Applicants respectfully request the Office continue to hold the obviousness-type double patenting rejection in abeyance until the present application is otherwise in condition for allowance.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this

application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

Patents and Applications

Applicants wish to draw the Examiner's attention to the following patents and/or applications. Applicants encourage the Examiner to review and monitor the prosecution of the following patents and/or applications, including all Office Actions, throughout the pendency of this application.

Patent / Serial Number	Title	Issued / Filed
10/793,497	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	03.04.2004
6,747,014	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	06.08.2004
09/315,298	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	05.20.1999
11/237,063	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	09.28.2005
6,169,079	OLIGONUCLEOTIDE INHIBITION OF CELL ADHESION	01.02.2001
6,300,491	OLIGONUCLEOTIDE INHIBITION OF CELL ADHESION	10.09.2001
09/659,288	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	09.12.2000
6,093,811	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	07.25.2000
6,015,894	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	01.18.2000
5,843,738	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	12.01.1998
6,096,722	ANTISENSE MODULATION OF CELL ADHESION MOLECULE EXPRESSION AND TREATMENT OF CELL ADHESION MOLECULE-ASSOCIATED DISEASES	08.01.2000
6,111,094	ENHANCED ANTISENSE MODULATION OF ICAM-1	08.29.2000
10/454,663	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	06.04.2003
6,849,612	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	02.01.2005
6,887,906	COMPOSITIONS AND METHODS FOR THE DELIVERY OF OLIGONUCLEOTIDES VIA THE ALIMENTARY CANAL	05.03.2005

08/886,829	COMPOSITIONS AND METHODS FOR THE DELIVERY OF OLIGONUCLEOTIDES VIA THE ALIMENTARY CANAL	07.01.1997
07/939,855	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	09.02.1992
5,591,623	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	01.07.1997
5,514,788	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	05.07.1996
5,883,082	COMPOSITIONS AND METHODS FOR PREVENTING AND TREATING ALLOGRAFT REJECTION	03.16.1999
07/567,286	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	08.14.1990
10/559,401	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	N/A
09/659,288	OLIGONUCLEOTIDE MODULATION OF CELL ADHESION	09.12.2000
09/082,624	COMPOSITIONS AND METHODS FOR NON-PARENTAL DELIVERY OF OLIGONUCLEOTIDES	05.21.1998

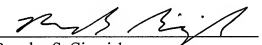
CONCLUSION

Applicants submit that the present application is in condition for allowance and respectfully requests an action to that effect. If any issues remain, the Examiner is invited to contact Applicants' counsel at the number provided below in order to resolve such issues promptly. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 9/24/10

By: 

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